REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Official Action dated June 27, 2003. In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Status of the Claims

Claims 6-8 and 10-11 are under consideration in this application. Claims 1-5 and 9 are being cancelled without prejudice or disclaimer. Claims 6-8 are being amended, as set forth in the above marked-up presentation of the claim amendments, in order to more particularly define and distinctly claim applicants' invention. New claims 10-11 are being added to recite other embodiments described in the specification.

Additional Amendments

The Title and the claims are being amended to correct formal errors and/or to better disclose or describe the features of the present invention as claimed. All the amendments to the claims are supported by the specification. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

Formality Rejections

Claim 9 was rejected under 35 U.S.C. §101, drawn to a "service", as being a non-statutory subject matter, and claims 1-3 and 9 were rejected under 35 U.S.C. § 112, second paragraph as being vague and indefinite. As claims 1-3 and 9 are being cancelled, the rejection becomes moot.

The title was objected to as being non-descriptive. As indicated, the Title has been amended as required by the Examiner. Accordingly, the withdrawal of the outstanding informality rejections is in order, and is therefore respectfully solicited.

Allowable Subject Matter

Claim 7 would be allowed if it is rewritten in an independent form to include all of the limitations of the base claim and any intervening claims.

Prior Art Rejections

Claims 1-2 and 5 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Pat. No. 5,834,286 to Nevalainen et al. (hereinafter "Nevalainen") or U.S. Pat. No. 6,162,900 to Guerinot et al. (hereinafter "Guerinot"). In addition, the Examiner rejected claim 6 as being anticipated by U.S. Pat. No. 6,110,710 to Smith et al. (hereinafter "Smith"). Claims 3 and 4 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Nevalainen or Guerinot, and claims 8 and 9 were rejected as being unpatentable over Smith. The prior art reference of Haff (2003/0039976) was cited as being pertinent to the present application. These rejections have been carefully considered, but are most respectfully traversed.

The method for determining a base sequence of a primer, as now recited in claim 6, comprises: carrying out a PCR by using four types of primers which respectively have a structure comprising a first sequence of a given base length complementary to one of single strands of a target DNA and a second sequence of a given base length provided adjacent to the side of 5' terminus of said first sequence and being non-complementary to the one of single strands of the target; analyzing results of amplified products obtained by the PCR; requiring efficiencies of adenylation using results of the step of analyzing; and determining one out of the four types of primers as a sequence which is most likely to undergo adenylation, wherein each of the four types of primers have one base at 5' terminus of the second sequence, the one base being different among the four types of primers. As such, the invention determines the sequence of a primer which preferentially brings an adenylated amplified product (page 4, line 11; page 6, lines 25 – 26)

The invention, as now recited in claim 8, is also directed to a method for determining a base sequence of a primer comprising: storing data of *anchor sequences* (defined on page 5, 2nd paragraph) whose adenylation efficiencies are preliminarily calculated based upon results of a PCR by using four types of primers which respectively have a structure comprising a first sequence of a given base length complementary to one of single strands of a target DNA and an anchor sequence of a given base length provided adjacent to the side of 5' terminus of said first sequence and being non-complementary to one single strands of the target DNA; inputting a sequence of the target DNA; determining an amplification area in the target DNA; designing a forward primer and a reverse primer corresponding to the amplification; extracting the anchor

sequence from the data stored in the step of storing data; designing an anchored reverse primer by adding the anchor sequence and the reverse primer; and calculating probabilities of a secondary structure formation between/inside the forward primer and the reverse primer and the anchored reverse primer. As such, the invention not only determines the sequence of a primer which preferentially brings an adenylated amplified product (page 4, line 11; page 6, lines 25 – 26), but also decide one out of a plurality of anchor sequences which is capable of giving a high efficiency of adenylation (line 18-21 page 27).

The invention, as now recited in claim 11, is further directed to a method for making primers comprising: carrying out a PCR by using four types of primers which respectively have a first sequence of a given base length complementary to one of single strands of a target DNA and a second sequence of a given base length provided adjacent to the side of 5' terminus of the first sequence and being non-complementary to the one of single strands of the target DNA; analyzing results of amplified products obtained by the PCR; requiring efficiencies of adenylation using results of the step of analyzing; determining one out of the four types of primers as a primer sequence which is most likely to undergo adenylation; and synthesizing primers having the primer sequence determined in the step of determining one out of the four types of primers, wherein each of the four types of primers have one base at 5' terminus of the second sequence, the one base being different among the four types of primers. As such, the invention makes primers which preferentially bring adenylated amplified products (page 4, line 11; page 6, lines 25 – 26).

Applicants respectfully contend that none of the cited references teaches or suggests a method including (1) a step of determining one out of four types of primers as a sequence which is most likely to undergo adenylation (Claims 6 and 11); (2) a step of storing data of anchor sequences whose adenylation efficiencies are preliminary calculated using a result of PCR by using four types of primers (Claim 8); or (3) a step of synthesizing primers having the sequence determined as most likely to undergo adenylation (Claim 11).

Smith was relied upon by the Examiner to teach a step of deciding which non-complementary sequence is most likely to undergo adenylation (page 4, paragraph 5 of the outstanding Office Action). Smith merely describes methods for resisting or promoting template independent nucleotide addition to the 3' terminus of a DNA duplex (Abstract). Smith amplifies a target using a primer comprising the 5' terminal sequence 5'-G-T-K-N-3' (K is G or T/U, N is A, C, G or T/U), and at least one of said terminal sequence residues is not complementary to

the target (Col. 1, lines 57 – 61). The sequence list regarding the consensus for resistance of adenylation is shown in Table 1, and the modifying tails favoring adenylation are listed in Figure 1. However, Smith fails to teach how to select the candidate sequences most favoring adenylation (Col. 7 and 8) such that it does not teach any of the steps (1)-(3).

Nevalainen and Guerinot fail to compensate for Smith's deficiencies. Nevalainen merely describes a recombinant strain which is capable of over-expressing at least two different genes under two separate promoters in filamentous fungi (Abstract). As the examiner commented, the primers have the sequence GA at the 5'-end (Col. 30, lines 43 – 46). The primers, "UPPHOS and DOWNPHOS," were inversely oriented and separated by 978 bases in genomic clones (Col. 30, lines 47-48). Nevalainen simply does not teach any of the steps (1)-(3).

Guerinot describes isolated nucleic acid molecules encoding novel members of the MRT family of polypeptides (Abstract). As the examiner commented, the primer has the sequence GG at the 5'-end (Col. 38, lines 5-16). However, this primer is totally complementary to a PCR fragment containing one part of ZRT1 sequence and BamHI restriction sites, and the primer is used in the step of transformation (Col. 37, lines 33-37). Guerinot just does not teach any of the steps (1)-(3).

As such, the present invention as now claimed in independent claims 6, 8 and 11 is distinguishable and thereby allowable over the rejections raised in the Office Action. The withdrawal of the outstanding prior art rejections is in order, and is respectfully solicited.

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art reference upon which the rejections in the Office Action rely, Applicant respectfully contends that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of

the above-captioned application, the Examiner is invited to contact the Applicants' undersigned representative at the address and phone number indicated below.

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September 15, 2003

SPF/JCM/JT